

Applicant : Ignatious, Francis *et al.*  
Serial No. : 09/171,740  
Filed : April 20, 1999  
Page : 6

#### **REMARKS**

This amendment is responsive to the Office Action mailed February 12, 2004. Original Claims 1, 4-21, 40 and 65 are under examination in the present action. Claims 1, 4-21, 40 and 65 stand rejected. No claim is allowed.

1. Applicants are grateful for the Examiner's withdrawal of the finality of the Office Action dated November 20, 2002 (Paper No. 26) and for the entry of their submission of December 22, 2003.

2-4. Claims 1, 4-21, 40 and 65 stand rejected under 35 U.S.C. §103(a) as being unpatentable over international application number PCT/US94/00148 (publication number WO 94/15587) (hereinafter referred to as "Shalaby"). Specifically, the Examiner contends the reference teaches the same process as that claimed in the instant application. In particular, the Examiner states that

Shalaby et al. disclose peptide-polymer ionic conjugate microparticles wherein the polymer is a polyester that is the same as the instant application. See pages 4-5 and 6-7, Tables 3, 6 and Example 11. The disclosed peptide is either LHRH or somatostatin. Example 11 of Shalaby teaches the instant methods. Ionic conjugates are formed by dissolving a biodegradable polymer in a liquid, while a peptide (drug) is dissolved in another liquid. These liquids are essentially mixed to form the peptide-polymer ionic conjugate and added to acetone. On page 4-5 and 6-7, Shalaby discloses that tetrahydrofuran (THF) or acetonitrile, or mixtures thereof is substituted for or with acetone.

Applicants readily admit that their claimed process utilizes the same ionic molecular conjugates of a polyester and a drug as those claimed by Shalaby. See page 1, lines 14-15 and page 1,

Applicant : Ignatious, Francis *et al.*  
Serial No. : 09/171,740  
Filed : April 20, 1999  
Page : 7

line 23 to page 2, line 1. Applicants contend, however, that the present application is directed to a novel process of making microparticles of the conjugates claimed by Shalaby. In addition, Applicants admit that Shalaby discloses that its claimed conjugates can be made into injectable microparticles. Applicants disagree, however, that the process to make such microparticles described in Shalaby is patentably similar to their process to make microparticles of the Shalaby conjugates. Shalaby at page 4, line 33, discusses a highly specific process to make said microparticles. In particular, the steps of the Shalaby process are as follows:

- (a) dissolving the composition in an aprotic, water miscible organic solvent;
- (b) mixing the organic solvent in water; and
- (c) isolating the microparticles from the water.

Shalaby provides a specific list of possible organic solvents that may be employed in the aforementioned process, namely acetone, acetonitrile, tetrahydrofuran, dimethylformamide and dimethoxy ethylene glycol. Shalaby, however, does not teach or suggest replacing water used in step (b) with any other liquid.

Without conceding the correctness of the Examiner's rejection and in an effort solely to better distinguish the present process from that disclosed by Shalaby, the Applicants have amended claim 1 to require that the solution comprised of the Shalaby conjugate and the organic solvent be introduced by way of an atomizing nozzle into either ethanol or isopropyl

Applicant : Ignatious, Francis *et al.*  
Serial No. : 09/171,740  
Filed : April 20, 1999  
Page : 8

alcohol and not water as required by Shalaby<sup>1</sup>. The Examiner's contention that "the acetone/peptide complex solution is ... injected into ... alcohol" as discussed on page 27, lines 3-4, is incorrect. Applicants contend that Example 11 of Shalaby clearly states that the complex solution is injected into "a rapidly stirring reservoir of 500 ml Milli-Q water at 4°C" and not alcohol as claimed by Examiner. Applicants respectfully contend that Shalaby requires that the conjugate-organic solvent solution must be introduced into water and that use of an alcohol was not anticipated by Shalaby.

The Applicants respectfully disagree with the Examiner's opinion that the temperature limitations of instant claim 11 are "not afforded patentable weight" since it would be "within the gambit of one skilled in the art to form the microparticles at a temperature that allowed for the quickest, most easily formed, or desirable microcapsules." Applicants contend that since Shalaby requires use of water as the medium in which the conjugates precipitate, that one skilled in the art would not appreciate having said medium at a temperature below 0°C. To better distinguish this difference, Applicants have amended claim 11 to lower the upper temperature limit to below 0°C.

Based on the foregoing, the Applicants respectfully submit that the Examiner has not made out a *prima facie* case of obviousness. It is well-established that an obviousness

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<sup>1</sup> This amendment has necessitated the cancellation of claim 10 without waiver or prejudice.

Applicant : Ignatious, Francis *et al.*  
Serial No. : 09/171,740  
Filed : April 20, 1999  
Page : 9

rejection be supported by some suggestion in prior art to create the claimed invention, to wit -

"[A] proper analysis under §103 requires, *inter alia*, consideration of . . . whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed invention",

*In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991) (emphasis added). As argued above, the Examiner has cited no prior art which would support such a suggestion in this case, i.e., that one of ordinary skill in the art should use either ethanol or isopropyl alcohol in a process to form microparticles of a sustained release ionic conjugate as claimed in the instant application. Accordingly, the rejection under 35 U.S.C. §103(a) is obviated and should be withdrawn.

5. The Examiner has rejected Applicants' arguments filed December 22, 2003 as not persuasive. Applicants contend that the Examiner used impermissible hindsight by rejecting the Applicants' argument on the grounds that "it is known in the art that syringes equipped with Teflon filters are used for injection of solutions via 0.2  $\mu$  Teflon filters ... [and that] [s]uch filter can be fitted with needles to produce small droplets." Use of a Teflon filter with a fitted needle is neither taught nor suggested by the one prior art reference cited by the Examiner. Applicants also assert that the onus is on the Examiner to show, using relevant prior art, that a Teflon filter with a fitted needle is patentably equivalent to the claimed atomizing nozzle. The teaching or suggestion to make the claimed combination and

Applicant : Ignatious, Francis *et al.*  
Serial No. : 09/171,740  
Filed : April 20, 1999  
Page : 10

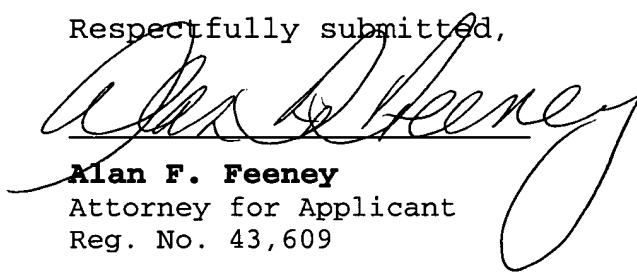
the reasonable expectation of success must both be found in the prior art and not based on the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Applicants respectfully request reconsideration of their arguments filed December 22, 2003.

Applicants respectfully submit that the claims are in a condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to telephone Applicant(s) attorney at (508) 478-0144 to facilitate prosecution of this application.

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